RAW SEQUENCE LISTING

The Biotechnology Systems Branch of the Scientific and Technical
Information Center (STIC) no errors detected.

Application Serial Number: _____ 10/658,355C _____

Source: _____ IFW 16 _____

Date Processed by STIC: _____ 11/15/2006 _____

ENTERED

IFW16

```
 3 <110> APPLICANT: Gantier, Rene
 4        Guyon, Thierry
 5        Hugo, Cruz Ramos
 6        Vega, Manuel
 7        Drittanti, Lila
 9 <120> TITLE OF INVENTION: Rational Directed Protein Evolution Using Two Dimensional
10        Rational Mutagenesis Scanning
12 <130> FILE REFERENCE: 17019-013001/923
14 <140> CURRENT APPLICATION NUMBER: US/10/658,355C
15 <141> CURRENT FILING DATE: 2003-09-08
17 <150> PRIOR APPLICATION NUMBER: 60/457,063
18 <151> PRIOR FILING DATE: 2003-03-21
20 <150> PRIOR APPLICATION NUMBER: 60/410,258
21 <151> PRIOR FILING DATE: 2002-09-09
23 <160> NUMBER OF SEQ ID NOS: 502
24 <170> SOFTWARE: FastSEQ for Windows Version 4.0
26 <210> SEQ ID NO: 1
27 <211> LENGTH: 165
28 <212> TYPE: PRT
29 <213> ORGANISM: Homo sapiens
31 <400> SEQUENCE: 1
32 Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
33  1               5                   10                  15
35 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
36              20                  25                  30
38 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
39          35                  40                  45
41 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
42      50                  55                  60
44 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
45 65                  70                  75                  80
47 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
48              85                  90                  95
50 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
51              100                 105                 110
53 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
54          115                 120                 125
56 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
57      130                 135                 140
59 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
60 145                 150                 155                 160
61 Leu Arg Ser Lys Glu
62              165
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CP9-67

RAW SEQUENCE LISTING   DATE: 11/15/2006
PATENT APPLICATION: US/10/658,355C   TIME: 11:44:02

Input Set : **F:\923SEQ.004.txt**
Output Set: **N:\CRF4\11152006\J658355C.raw**

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64 <210> SEQ ID NO: 2
65 <211> LENGTH: 165
66 <212> TYPE: PRT
67 <213> ORGANISM: Artificial Sequence
69 <220> FEATURE:
70 <223> OTHER INFORMATION: D2A Mutant INF-alpha 2b
72 <400> SEQUENCE: 2
73 Cys Ala Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
74 1               5                   10                  15
76 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
77             20                  25                  30
79 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
80         35.                 40                  45
82 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
83     50                  55                  60
85 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
86 65                  70                  75                  80
88 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
89             85                  90                  95
91 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
92             100                 105                 110
94 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
95         115                 120                 125
97 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
98     130                 135                 140
100 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
101 145                 150                 155                 160
102 Leu Arg Ser Lys Glu
103                 165
105 <210> SEQ ID NO: 3
106 <211> LENGTH: 165
107 <212> TYPE: PRT
108 <213> ORGANISM: Artificial Sequence
110 <220> FEATURE:
111 <223> OTHER INFORMATION: P4A Mutant INF-alpha 2b
113 <400> SEQUENCE: 3
114 Cys Asp Leu Ala Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
115 1               5                   10                  15
117 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
118             20                  25                  30
120 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
121             35                  40                  45
123 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
124     50                  55                  60
126 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
127 65                  70                  75                  80
129 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
130             85                  90                  95
132 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
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RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/658,355C

DATE: 11/15/2006
TIME: 11:44:02

Input Set : F:\923SEQ.004.txt
Output Set: N:\CRF4\11152006\J658355C.raw

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133             100             105             110
135 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
136         115             120             125
138 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
139     130             135         ,   140
141 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
142 145             150             155             160
143 Leu Arg Ser Lys Glu
144             165
146 <210> SEQ ID NO: 4
147 <211> LENGTH: 165
148 <212> TYPE: PRT
149 <213> ORGANISM: Artificial Sequence
151 <220> FEATURE:
152 <223> OTHER INFORMATION: Q5A Mutant INF-alpha 2b
154 <400> SEQUENCE: 4
155 Cys Asp Leu Pro Ala Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
156 1           5               10              15
158 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
159         20              25              30
161 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
162         35              40              45
164 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
165     50              55              60
167 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
168 65              70              75              80
170 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
171             85              90·             95
173 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
174         100             105             110
176 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
177         115             120             125
179 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
180     130             135             140
182 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
183 145             150             155             160
184 Leu Arg Ser Lys Glu
185             165
187 <210> SEQ ID NO: 5
188 <211> LENGTH: 165
189 <212> TYPE: PRT
190 <213> ORGANISM: Artificial Sequence
192 <220> FEATURE:
193 <223> OTHER INFORMATION: T6A Mutant INF-alpha 2b
195 <400> SEQUENCE: 5
196 Cys Asp Leu Pro Gln Ala His Ser Leu Gly Ser Arg Arg Thr Leu Met
197 1           5               10              15
199 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
200         20              25              30
```

```
202 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
203     35              40              45
205 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
206     50              55              60
208 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
209 65              70              75              80
211 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
212             85              90              95
214 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
215             100             105             110
217 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
218         115             120             125
220 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
221     130             135             140
223 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
224 145             150             155             160
225 Leu Arg Ser Lys Glu
226                 165
228 <210> SEQ ID NO: 6
229 <211> LENGTH: 165
230 <212> TYPE: PRT
231 <213> ORGANISM: Artificial Sequence
233 <220> FEATURE:
234 <223> OTHER INFORMATION: H7A Mutant INF-alpha 2b
236 <400> SEQUENCE: 6
237 Cys Asp Leu Pro Gln Thr Ala Ser Leu Gly Ser Arg Arg Thr Leu Met
238 1               5               10              15
240 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
241             20              25              30
243 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
244         35              40              45
246 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
247     50              55              60
249 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
250 65              70              75              80
252 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
253             85              90              95
255 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
256             100             105             110
258 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
259         115             120             125
261 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
262     130             135             140
264 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
265 145             150             155             160
266 Leu Arg Ser Lys Glu
267                 165
269 <210> SEQ ID NO: 7
270 <211> LENGTH: 165
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RAW SEQUENCE LISTING   DATE: 11/15/2006
PATENT APPLICATION: US/10/658,355C   TIME: 11:44:02

Input Set : **F:\923SEQ.004.txt**
Output Set: **N:\CRF4\11152006\J658355C.raw**

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271 <212> TYPE: PRT
272 <213> ORGANISM: Artificial Sequence
274 <220> FEATURE:
275 <223> OTHER INFORMATION: S8A Mutant INF-alpha 2b
277 <400> SEQUENCE: 7
278 Cys Asp Leu Pro Gln Thr His Ala Leu Gly Ser Arg Arg Thr Leu Met
279 1               5               10              15
281 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
282             20              25              30
284 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
285         35              40              45
287 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
288     50              55              60
290 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
291 65              70              75              80
293 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
294             85              90              95
296 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
297             100             105             110
299 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
300             115             120             125
302 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
303     130             135             140
305 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
306 145             150             155             160
307 Leu Arg Ser Lys Glu
308             165
310 <210> SEQ ID NO: 8
311 <211> LENGTH: 165
312 <212> TYPE: PRT
313 <213> ORGANISM: Artificial Sequence
315 <220> FEATURE:
316 <223> OTHER INFORMATION: L9A Mutant INF-alpha 2b
318 <400> SEQUENCE: 8
319 Cys Asp Leu Pro Gln Thr His Ser Ala Gly Ser Arg Arg Thr Leu Met
320 1               5               10              15
322 Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
323             20              25              30
325 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
326         35              40              45
328 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
329     50              55              60
331 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
332 65              70              75              80
334 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
335             85              90              95
337 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
338             100             105             110
340 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
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RAW SEQUENCE LISTING ERROR SUMMARY DATE: 11/15/2006
PATENT APPLICATION: US/10/658,355C TIME: 11:44:03

Input Set : F:\923SEQ.004.txt
Output Set: N:\CRF4\11152006\J658355C.raw

Please Note:
Use of n and/or Xaa have been detected in the Sequence Listing. Please review the
Sequence Listing to ensure that a corresponding explanation is presented in the <220>
to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:195; N Pos. 1,22

VERIFICATION SUMMARY   DATE: 11/15/2006
PATENT APPLICATION: **US/10/658,355C**   TIME: 11:44:03

Input Set : **F:\923SEQ.004.txt**
Output Set: **N:\CRF4\11152006\J658355C.raw**

L:7601 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:195 after pos.:0